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CASE REPORT

Multiple endocrine neoplasia type 2A

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Abstract Multiple endocrine neoplasia type 2A (MEN 2A) is an autosomal dominant inherited cancer syndrome that expresses nonendocrine and endocrine tumors. Here, we describe a 42-year-old man with an initial presentation of low back pain and hypertension. Clinical assessments revealed pheochromocytoma, medullary thyroid carcinoma with bone metastasis, and parathyroid hyperplasia. MEN 2A was diagnosed, and a family history of pheochromocytoma was traced. Surgical resection of the pheochromocytoma of the adrenal gland resulted in a cure of the patient's hypertension. He received systemic chemotherapy with the "MAID" regimen (mesna, doxorubicin, ifosfamide, and dacarbazine) over three cycles of 3 weeks each, and showed a partial response.

Introduction

Multiple endocrine neoplasia (MEN) is an autosomal dominant inherited cancer syndrome with a prevalence rate of 2.5 per 100,000 individuals in the general population [1]. MEN type 2 comprises medullary thyroid carcinoma, pheochromocytoma, and parathyroid hyperplasia or adenoma. A mutation in the *RET* proto-oncogene, which encodes a tyrosine receptor, is associated with the MEN 2 family [1].

We present the case of a 42-year-old male patient who had MEN 2A and a family history that contributed to the development of the syndrome. His mother had a history of pheochromocytomas and a thyroid tumor of unknown cell type. Surgical resection of the pheochromocytoma in the patient's adrenal gland resulted in a cure of his hypertension. He received systemic chemotherapy with the "MAID" regimen (mesna, doxorubicin, ifosfamide, and dacarbazine) over three cycles of 3 weeks each, and showed a partial response.

Case report

A 42-year-old man who had had chronic hepatitis B and hypertension for 10 years presented with low back pain, which he had been experiencing for 1 week, accompanied by weight loss of 3–5 kg over the preceding 2 months, headache, and paradoxical sweating. His baseline blood pressure was 200/100 mmHg.

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Figure 1. Magnetic resonance imaging (MRI) of the spine showed multiple metastases within the vertebral bodies of the T8—L5 vertebrae, spinous processes, sacrum, and iliac bones.

Because of the low back pain, he underwent spine radiography, which revealed a compression fracture from T12 to L2, and magnetic resonance imaging of the spine showed multiple metastases within the vertebral bodies of the T8—L5 vertebrae, spinous processes, sacrum, and iliac bones (Fig. 1). The initial laboratory findings are shown in Table 1.

Abdominal echo revealed a left adrenal mass (4.8 cm × 5.1 cm; Fig. 2A). The computed tomography scan of the abdomen showed a left adrenal mass (4.8cm × 5.1 cm), which showed the same lesion compatible with abdominal echo finding. (Fig. 2B). Thyroid ultrasonography revealed a multinodular goiter; the right side of the thyroid gland measured 1.2 cm × 0.6 cm (Fig. 3A) and the left side 4.6 cm × 1.98 cm (Fig. 3B). Because of hypertension associated with the left-sided adrenal tumor mass, we consulted a urologist to debulk the left-sided adrenal gland tumor.

Pathological analysis of the adrenal gland tumor showed a "ball in the hole"-like tumor nest separated by epithelial cells or a trabecular architecture, which is known as a zellballen arrangement [2] and is characteristic of pheochromocytomas (Fig. 4A). Furthermore, immunohistochemical studies showed positivity for chromogranin A (Fig. 4B). The patient underwent total thyroidectomy, and pathological analysis of the thyroid tumor showed round to oval-shaped tumor cells with a salt and pepper-like appearance (Fig. 4C). Immunohistochemical studies also showed positivity for calcitonin (Fig. 4D).

The patient received a thoracic spine (T spine) bone biopsy, which showed the presence of a thyroid tumor (data not shown) characteristic of medullary thyroid carcinoma. The parathyroid gland showed mild hyperplasia (data not shown). Taken together, the patient presented with evidence of medullary thyroid carcinoma with bone metastasis, primary hyperparathyroidism, and pheochromocytoma, and the diagnosis was MEN 2A.

Surgical resection of the pheochromocytoma in the left-sided adrenal gland resulted in a cure of the patient's hypertension. He received systemic chemotherapy with the "MAID" regimen (mesna, doxorubicin, ifosfamide, and dacarbazine) over three cycles of 3 weeks each, and showed a partial response. The patient's hypertension and vanillylmandelic acid levels recovered to normal ranges. The laboratory of calcitonin showed a partial response (Table 1).

Discussion

MEN 2 is a rare autosomal dominant disease. In an original article describing MEN 2A patients, the prognosis of this

Table 1 Results of laboratory tests.

Variable	Reference range	Initial laboratory	Post chemotherapy
Hematocrit (%)	41.5—50 (male)	45	43
Hemoglobin (g/dL)	14—17.5 (male)	14.1	13
White cell count (/mm^3)	4,400—11,300 (male)	13,370	8,000
Platelet count (/mm^3)	172,000—450,000	279000	260,000
Vanillylmandelic acid (mg/24 h)	<6	25.1	<5
Calcitonin (pg/mL)	<12	606.3	300
Parathyroid hormone (pg/mL)	11—54	66	50
Iron calcium (mg/dL)	4.6—5.2	5.5	4.8
Phosphate (mg/dL)	2.5—4.6	2.4	3.1
Blood urea nitrogen(mg/dl)/creatinine (mg/dl)	8—20/0.6—1.3	14.1/0.6	15/0.8
GOT/GPT (IU/L)	10—40	48/50	44/48
Sodium (mmol/L)	136—144	137	130
Potassium (mmol/L)	3.5—5.1	4.5	4.2

GOT = aspartate aminotransferase; GPT = alanine aminotransferase.

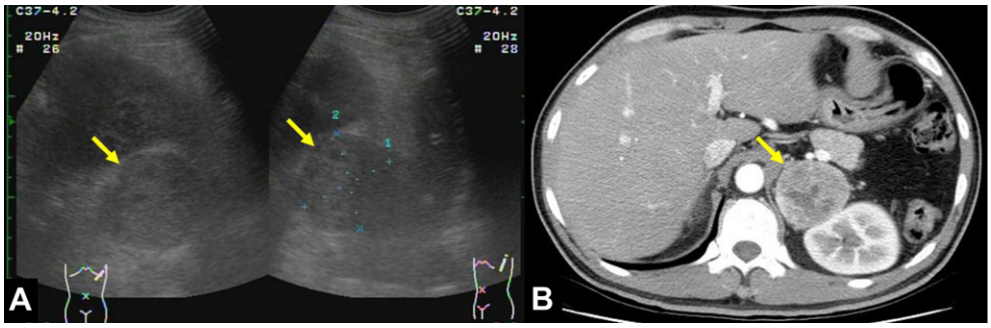

Figure 2. (A) Abdominal echo revealed a left adrenal mass (4.8 × 5.1 cm). (B) Computed tomography (CT) scan of the abdomen showed the same lesion.

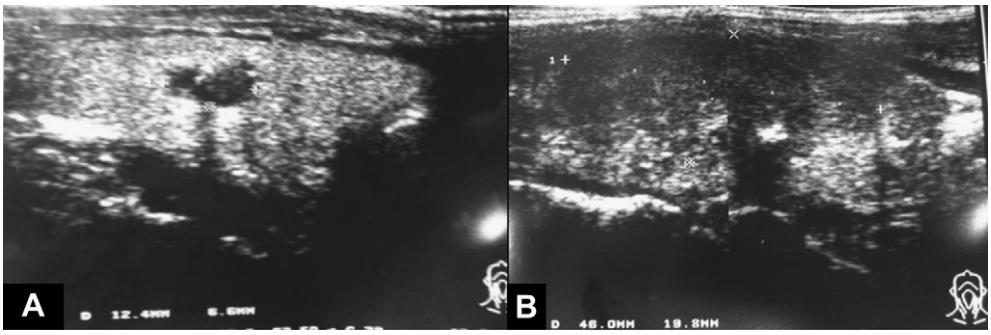

Figure 3. (A) Thyroid ultrasonography showed right-side tumor mass (1.2 × 0.6 cm). (B) Thyroid ultrasonography showed left-side tumor mass (4.6 × 1.98 cm).

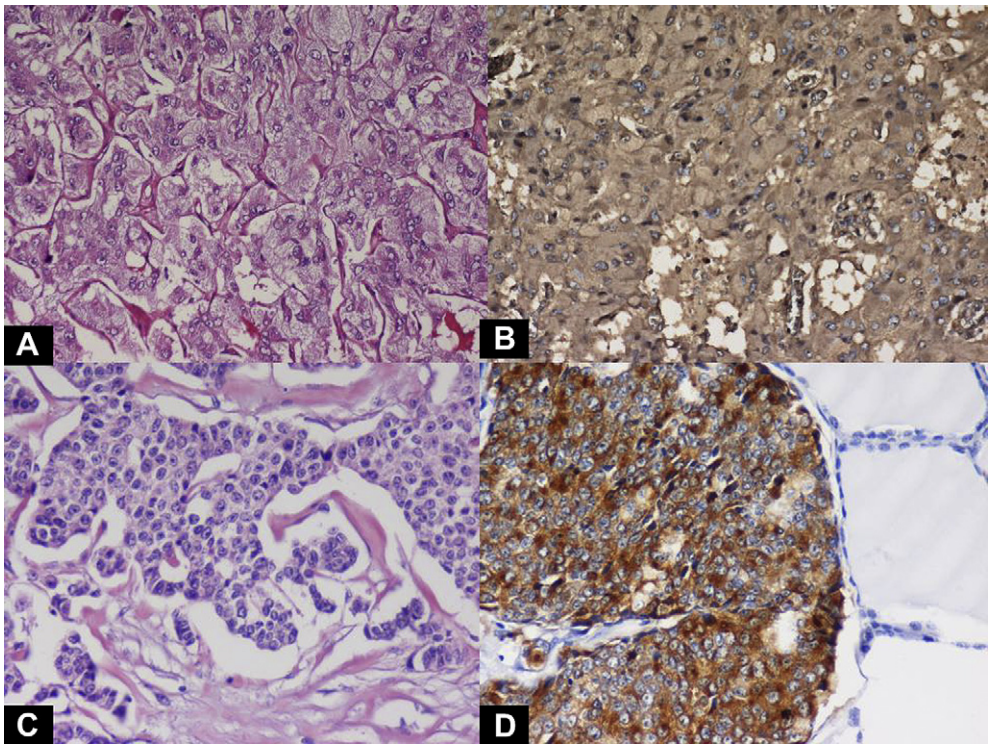

Figure 4. (A) Pathological analysis of the adrenal gland tumor showed a ball-in-hole-like tumor nest that was separated by epithelium cells or trabecular architecture, which is known as the "zellballen arrangement" and is characteristic of pheochromocytoma with vascular permeation. (B) Immunohistochemical studies of the adrenal gland tumor showed positivity for chromogranin-A. (C) Pathological analysis of the thyroid tumor showed round-to-oval-shaped tumor cells with salt- and pepper-like appearance. (D) Immunohistochemical studies of the thyroid tumor showed positivity for calcitonin.

mutation in Cys codons 609, 611, 618, 620, and 634 was discussed [3]. Early diagnosis by screening family members for MEN 2A kindreds is essential because medullary thyroid carcinoma is a life-threatening disease that can be cured or prevented by performing early thyroidectomy [3].

Marijuan et al. discussed prophylactic thyroidectomy for patients with MEN 2A who were screened for *RET* mutations [4]. We reviewed the efficacy of systemic chemotherapy for advanced medullary thyroid carcinoma [5—8]. All of the regimens achieved a partial response, but complete remission was achieved in only a few cases. Alternative treatments included the administration of biologic modifiers and radioimmunotherapy [9].

The patient described here received systemic chemotherapy with the "MAID" over three cycles of 3 weeks each, and obtained a partial response. After debulking of the pheochromocytoma in the left-sided adrenal gland, the patient's hypertension and vanillylmandelic acid level recovered to normal ranges, and the laboratory calcitonin result showed a partial response.

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